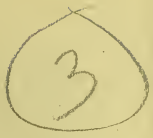

CHEMISTRY

IN ITS

RELATIONS TO THERAPEUTICS.

THE subject of Chemistry in its relations to Therapeutics is one which should possess considerable interest for every member of the profession of medicine. I suppose there is not one of us who does not welcome every effort towards establishing therapeutics on a scientific basis.

My present object is to direct attention to certain recent chemico-therapeutical researches which are of no little importance as serving in some degree to raise therapeutics from the grade of irrational empiricism to the dignity of an exact science.

Three lines of research, although as yet imperfectly prosecuted, have already borne fruit, and hold out promises of an abundant harvest; these enquiries are—1st. The chemistry of the tissues and secretions in their healthy and morbid states; 2nd. The connection between the chemical constitution and physiological action of medicinal agents; and 3rd. The chemical decomposition and alteration of drugs in the animal economy.

To the chemist undoubtedly belongs the credit of paving the way to a scientific therapeutic method. "Chemical enquiry is now finding its way into many of the remoter secrets of function, and is likely before long to establish some laws of molecular constitution which will enable us to classify unknown remedies and to explain and calculate their actions." So writes Clifford Allbutt.

The necessity of studying remedies from their chemical relation to the animal tissues is forcibly indicated by Charles Bland Radcliffe in his paper on "The Treatment of Neuralgia," read before the British Medical Association, at the Bristol meeting in 1863. He reasons thus: Nerve pain is indicative of deterioration of nerve tissue; hence phosphorus and cod-liver oil as nutrients for the nerve tissue are the appropriate remedies.

So long ago as 1841, Blake (*a*) attempted to frame a law to the effect that salts of isomorphous bases have in general a similar action. So far as I am aware, this was the first attempt to define a connection between chemical constitution and therapeutic action.

In 1868 Dr. W. H. Broadbent brought an extremely interesting communication under the notice of the Royal Society of London. (*b*) In this paper the author states that "substances chemically allied should have similar physiological and therapeutic actions, or any diversity found to exist should be capable of explanation on chemical grounds." The source of nerve-force is stated to be oxidation, and the seat of oxidation is the nervous structures. Poisons which kill by their action on the nervous system all contain nitrogen, and this element is the pivot on which the deadly influence turns. In the nervous structures carbon and hydrogen are liberated in the nascent state and appropriate the oxygen brought by the blood, and thus produce a result equivalent to exclusion of oxygen. The carbon and hydrogen are set free by the dislocating influence ("chemical tension") of nitrogen. Prussic acid affords a striking example of a poison acting in such a manner. This paper of Broadbent's is eminently suggestive, and must be regarded as a valuable contribution to the chemistry of therapeutics. I have now to ask attention to the masterly essay of Drs. Crum Brown and Thomas Fraser, "On the Connection between Chemical Constitution and Physiological Action." (*c*) These investigators show that composition alone is insufficient to explain physiological action, and that constitution, by which is meant the mutual relations of the atoms in a substance, must also be taken into account. Thus, acetic acid and sugar are identical in composition, as are glycocoll and nitrite of ethyl; again, kakodylic acid is inert, although it is perfectly soluble and contains 54 per cent. of metallic arsenic. It would be foreign to my pur-

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(*a*) "Proceedings of the Royal Society of London," vol. iv., Jan. 28th, 1841.

(*b*) "An Attempt to apply Chemical Principles in Explanation of the Action of Poisons." ("Proceedings of the Royal Society of London." vol., xvi., 1868.)

(*c*) "Transactions of the Royal Society of Edinburgh," vol. xxv.

pose to enter into anything like an elaborate analysis of this valuable paper. I will content myself by stating that the learned authors have shown that the physiological action of a substance may be completely altered by introducing into it a definite chemical change without breaking up its molecule. Thus, by adding iodide of methyl to the non-saturated base, strychnia, its poisonous properties were greatly diminished. The authors conclude that while "physiological activity is related to condensation, the occurrence of saturated substances such as alcohol, corrosive sublimate, and oxalic acid, having a well-marked poisonous action, and of condensed substances such as benzoic acid and salicine, which are comparatively inert, shows that condensation is not the only condition of physiological activity. There can, at the same time, be little doubt, that if the effect of condensation were discovered and eliminated, the other conditions might be much more hopefully sought for."

While Crum Brown and Fraser were thus working in this country, Jolyet and Cahours were pursuing an almost identical line of investigation on the Continent. (*a*) Knowing that in various compounds an equivalent of hydrogen may be substituted by an organic radical without chemically changing the fundamental properties of the original compound, they investigated the question as to whether this substitution would modify the physiological properties of the compound. They compared the action of aniline with that of ethyl-aniline, trimethyl-aniline, and amyl-aniline. They found that while the action of aniline is to excite the cerebro-spinal centres so as to produce convulsions, the action of the derivatives was to abolish the function of those centres. One of the most definite chemico-therapeutical laws has recently been enunciated by Rabuteau. It is to the effect that metals are more active physiologically according as their atomic weights are higher or as their specific heats are lower. This law holds good as regards the diatomic metalloids, but the monatomic metalloids are governed by a law which is the reverse of this. The metals rubidium, tungsten, and molybdenum form exceptions to this law. I should not pass over the fact that M. Rabuteau has proved that the organism is a reducing agent converting bromates into bromides, sulphates into sulphites and hyposulphites, and so forth.

B. Ward Richardson has done good service in drawing attention to the connection between chemical constitution and physiological action as evidenced by the alcohols. The number of atoms of carbon contained in an alcohol would seem to serve as an index to its activity; thus, ethylic

(*a*) "On the Substitution Compounds of Aniline." (Comptes Rendus, tome lxvi., 1868, p. 1131.)

alcohol contains but two atoms of carbon, while amylic alcohol, which is much more active, has five atoms.

I purpose now to direct attention to certain theorems which that advanced therapeutist, M. Gubler, has recently advanced relative to the sphere of action and of elimination of drugs.(*a*) I say "theorems," for, for lack of absolute proof, we cannot assign to these propositions the standard of definite laws. The first of these axioms or theorems may thus be stated: Substances tend towards their similars or analogues in the animal economy—thus, sulphur would tend towards sulphur, phosphorus towards phosphorus, arsenic towards phosphorus, bromine towards chlorine, selenium towards sulphur and so on. A second theorem is that when a substance cannot meet with its similar or analogue it cannot be assimilated, and must be eliminated. A third proposition is that a substance is eliminated by that channel in which it meets with similar bodies—thus, neutral salts, sulphocyanide of potassium and soda, would be eliminated by the *saliva* and *pancreatic juice;* soda, fatty acids, neutral fatty bodies, cholesterin, resin, and ferruginous pigment by the *bile;* neutral salts, substances acting as acids, fatty matters, water, and ferruginous pigment by the *urine;* gas and vapours by the *breath;* casein, lactine volatile fatty acids, butter, and neutral salts by the *milk*; and fatty acids, volatile acids, and neutral salts by the *sweat.* For my own part I am inclined to regard these theorems as in the main verging on absolute truth, and until they are disproved, or until some equally intelligible and plausible proposition is offered, I will elect to regard these axioms of Gubler as adequately explanatory of the sphere of action and of the channel of elimination of drugs. I lean strongly to the opinion that the presence of quiniodine in animal tissues, as has been demonstrated by the masterly researches of Bence Jones and Dupré, is a powerful argument in favour of Gubler's views.

I will now briefly allude to a subject of considerable interest which M. Onimus has recently brought under the notice of the Académie des Sciences. That investigator finds that the interposition of a layer of some albuminoid substance, as the white of an egg, between two liquids, often gives rise to electro-chemical phenomena. If into an U-shaped tube some albumen be poured, and if into one side a solution of sulphate of copper be placed, and into the other side a solution of oxalate of potash, after a while blue crystals of double oxalate of copper and potash will be formed. Again, when phosphate of soda is placed in one side, and chloride

(*a*) See an article by M. Bordier in the *Bulletin de Thérapeutique* January 30th, 1873.

of lime in the other, phosphate of lime will be obtained in the side in which the phosphate of soda was placed. These facts are not without therapeutical application, for we may infer that it would be more beneficial to administer these salts separately than to give phosphate of lime directly, since this salt is so easily formed in the organism.

The discovery of the physiological action of chloral by the illustrious Liebrich has given such an impetus to the study of the decomposition of chemical agents in the organism that it is probable this line of research will ere long extend to the whole course of therapeutical learning. The attention of the Académie des Sciences has lately been occupied by the extremely interesting researches of M. Byasson and M. Personne relative to the chemico-physiological action of chloral. In the "Monthly Reports on the Progress of Therapeutics," which I have the honour to edit for the *Edinburgh Medical Journal*, I have not omitted to refer to these investigations. M. Byasson thinks that the longer duration of the action of chloral compared with that of chloroform is due to the slowness of the chemical action, and that the difference in the physiological phenomena is explained by the intervention of formic acid produced at the same time as the chloroform, and acting under special conditions. M. Personne, on the other hand, is of opinion that the combination of the chloral with albumen explains the longer duration of action of this body compared with chloroform. The first action of chloral on the albuminoid materials of the economy produces chloroform at the expense of their alkali; at the same time, these materials, deprived of their alkali, contract a combination with the undestroyed chloral, and this combination is, in some sort, a reservoir of chloroform. Thus is explained why it is we meet with so small a quantity of chloroform in the blood of animals submitted to the action of chloral. The theory that the action of chloral is in part to be accounted for on the supposition that formic acid is produced, and is subsequently reduced into carbonic acid in the system, M. Personne has endeavoured to disprove experimentally. He gave formic acid to dogs without perceiving the slightest production of carbonic acid, nor did any symptoms of anæsthesia supervene.

I have now briefly glanced at some important chemico-therapeutical researches which have recently occupied the attention of scientists. I trust on a future occasion to bring forward a more ample statement, and to formulate some additional laws which my own researches would seem to warrant, but the enunciation of which in their present stage would be premature.

It will be seen from what I have stated that I am an ardent disciple of the School of Chemical Therapeutics. I

must be understood, however, to advocate as ardently physiological and clinical research. The labours of the chemist will be unavailing if not co-existent with the researches of the physiologist, and both must be supplemented by the careful observations of the clinical physician.

The flood of light which is being shed upon the nature of diseased action by the labours of the physiologist and pathologist, the modern refinements of clinical investigation, and the impetuous progress of chemical science will ere long bear fruit in the establishment of a therapeutic method worthy the name of science. Have not the researches which I have brought under notice an importance as evidencing a line of investigation pregnant with golden promises? May it not be that the generation to come will look back on the empiricism of to-day as do we on the pretensions of the past?

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